UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,924	01/17/2006	Roberto Crea	CREA-001US	2319

51951 7590 04/02/2009

THE LUTHER LAW FIRM, PLC
10575 N 114TH STREET
SUITE 103
SCOTTSDALE, AZ 85259

EXAMINER	
FLOOD, MICHELE C	
ART UNIT	PAPER NUMBER
1655	

MAIL DATE	DELIVERY MODE
04/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,924	CREA, ROBERTO	
	Examiner	Art Unit	
	Michele Flood	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-8,13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/27/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the species of administration of an aqueous extract of olives readable on Claims 9-12 and 15-18 in the reply filed on January 12, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 9-12 and 15-18 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-12 and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 15 are deemed incomplete because the claims lack method steps. For instance, while the preamble of the claims recites a method of treating patients with large fiber and C-fiber neuropathy comprising administering a claim-designated ingredient(s), it is unclear as to the subject matter Applicant intends to direct the instantly claimed invention since there is no subject to which the claim-designated ingredients are administered to effect a result. The lack of clarity renders the claims

indefinite since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired.

The metes and bounds of Claims 10-12 and 16-18 are rendered indefinite by the phrase “a weight ratio of hydroxytyrosol to oleuropein of between about X:Y and about Z:X” because the simultaneous recitation of “between” and “about” fails to provide any specific indication as to what range of numerical value is covered by "between about". The lack of clarity renders the claims ambiguous.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 9-12 and 15-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Crea (A*; US 2004/0039066 A1).

Applicant claims a method of treating patients with large fiber and C-fiber neuropathy comprising administering an aqueous extract of olives. Applicant further claims the method of claim 9 wherein the aqueous extract of olives contains a weight ratio of hydroxytyrosol to oleuropein of between about 1:1 and about 400:1; wherein the aqueous extract of olives contains a weight ratio of hydroxytyrosol to oleuropein of

between about 3:1 and about 200:1; and, wherein the aqueous extract of olives contains a weight ratio of hydroxytyrosol to oleuropein of between about 5:1 and about 50:1.

Applicant claims a method of treating patients with large fiber and C-fiber neuropathy comprising administering an extract of an olive tree product selected from the group consisting of olive and olive leaf. Applicant further claims the method of claim 15 wherein the aqueous extract of olives contains a weight ratio of hydroxytyrosol to oleuropein of between about 1:1 and about 400:1; wherein the aqueous extract of olives contains a weight ratio of hydroxytyrosol to oleuropein of between about 3:1 and about 200:1; and, wherein the aqueous extract of olives contains a weight ratio of hydroxytyrosol to oleuropein of between about 5:1 and about 50:1.

Crea teaches treating an AIDS-associated neurological disorder in a subject comprising administering an effective amount of a composition comprising an aqueous extract of olives having a weight ratio of hydroxytyrosol to oleuropein of between about 1:1 and about 200:1 or between about 5:1 and about 100:1 or between 10:1 and about 50:1. *See* [0039]. At [01404]-[0109], Crea teaches that t he method is used for treating peripheral neuropathy. Although not expressly taught by Crea, AIDS-associated peripheral neuropathy is characterized by large fiber and C-fiber neuropathy. Thus, the claimed invention is inherent to the method taught by Crea because the ingredients, the amounts of the ingredients and the process steps are one and the same disclosed in the invention claimed by Applicant. . Moreover, the instantly claimed process is a one-step process of administering an aqueous extract of olives or administering an extract of

an olive tree product wherein the patient population or subject to which the administering is directed is unspecified.

The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hatake (N; Translation of foreign language patent provided herein.) in view of Bhadada et al. (U).

Applicant's claimed invention was set forth above.

Hatake teaches administering an effective amount of an aqueous extract of an olive leaf extract comprising 25% or more of oleuropein to a patient to provide a method

of controlling blood sugar level and depressing a rise in blood sugar level. *See* [0023]. At [0018], Hatake further teaches that the oleuropein-containing olive leaf extract exerts health promoting effect including plasma agglutination inhibition, phospholipid oxidation inhibition, serum glucose depressant action and LDL oxidation depressant action.

The teachings of Hatake as set forth above do not specifically teach a method of treating patients with large fiber and C-fiber neuropathy. However, it would have been obvious to one of ordinary skill in the art to administer the aqueous olive leaf extract taught by Hatake to patients with large fiber and C-fiber neuropathy to provide the instantly method of treatment because at the time the invention was made Bhadada taught that peripheral neuropathies are secondary to a number or metabolic and vascular conditions. In particular, Bhadada teaches that approximately 50% of patients with diabetes mellitus suffer from peripheral neuropathy that may affect the small myelinated fibers (C-fiber), causing loss of pain and temperature sensation, or the large fibers, causing motor or somatosensory defects. On page 307, Column 2, under "*Pathogenesis of diabetic neuropathy*", Bhadada further teaches that neuropathy in diabetes mellitus is a multifactorial disease and that possible etiologic factors contributing to its development include hyperglycaemia, polyol pathway, non-enzymatic glycation, free radical and oxidative stress' "Generally the nerve involvement has been correlated with glycaemic control, hyperglycaemia induced metabolic derangements and neurophysiological alterations, serum lipid changes, vascular coagulation, and thrombotic abnormalities [citation omitted]." At the time the invention was made, one of ordinary skill in the art would have been motivated and would have had a reasonable

expectation of success to administer the aqueous olive leaf extract taught by Hatake to patients with large fiber and C-fiber neuropathy to provide the claimed invention because Bhadada taught that control of blood sugar levels reduces the occurrence of clinical neuropathy (*See* page 310, Column 2, second paragraph) and that effective treatment of hyperglycemia is an important factor in delaying the progress of diabetic neuropathy; and, Hatake taught that administration of effective amounts the aqueous extract of olive leaf containing oleuropein not only depresses increases in blood sugar levels but also exerts action against other aetiologic factors suggested by Bhadada as factors contributing to the pathogenesis of diabetic neuropathy involving large fiber and C-fiber dysfunction.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bennani-Kabachi et al. (V) in view of Bhadada et al. (U), in light of Benavente-Garcia et al. (W).

Applicant's claimed invention was set forth above.

Bennani-Kabachi teaches administering an effective amount of an aqueous olive extract to patients induced with hypercholesterolemia. Bennani-Kabachi teaches that treatment with the plant extract showed hypoglycemic, antihyperglycaemic and

hypoinsulinaemic effects associated with decreased plasmin insulin, as well as reduced capillary thickening in skin and pancreas. Microangiopathy was also markedly reduced in the skin, and pancreas, and completely prevented in the kidneys.

Benavente-Garcia is relied upon to show that hydroxytyrosol and oleuropein are necessarily present in an aqueous extract of olive leaves.

The teachings of Bennani-Kabachi as set forth above do not specifically teach a method of treating patients with large fiber and C-fiber neuropathy. However, it would have been obvious to one of ordinary skill in the art to administer the aqueous olive leaf extract taught by Bennani-Kabachi to patients with large fiber and C-fiber neuropathy to provide the instantly claimed method of treatment because at the time the invention was made Bhadada taught that peripheral neuropathies are secondary to a number or metabolic and vascular conditions. In particular, Bhadada teaches that approximately 50% of patients with diabetes mellitus suffer from peripheral neuropathy that may affect the small myelinated fibers (C-fiber), causing loss of pain and temperature sensation, or the large fibers, causing motor or somatosensory defects. On page 307, Column 2, under "*Pathogenesis of diabetic neuropathy*", Bhadada further teaches that neuropathy in diabetes mellitus is a multifactorial disease and that possible aetiolgic factors contributing to its development include hyperglycaemia, polyol pathway, non-enzymatic glycation, free radical and oxidative stress' "Generally the nerve involvement has been correlated with glycaemic control, hyperglycaemia induced metabolic derangements and neurophysiological alterations, serum lipid changes, vascular coagulation, and thrombotic abnormalities [citation omitted]." On page 309, Bhadada further teaches that

vascular and haemorrheological abnormalities also contribute to the pathogenesis of diabetic neuropathy impairing microcirculation and increasing vasoconstriction. At the time the invention was made, one of ordinary skill in the art would have been motivated and would have had a reasonable expectation of success to administer the aqueous olive leaf extract taught by Bennani-Kabachi to patients with large fiber and C-fiber neuropathy to provide the claimed invention because Bhadada taught that control of blood sugar levels reduces the occurrence of clinical neuropathy (See page 310, Column 2, second paragraph) and that effective treatment of hyperglycemia is an important factor in delaying the progress of diabetic neuropathy; and, Bennani-Kabachi taught that administration of effective amounts of an aqueous extract of olive leaf not only provided a hypoglycemic effect but also reduced lipid peroxidation, lowered plasma fasting glucose, improved glucose tolerance and reduced microangiopathy, which are factors suggested by Bhadada as contributing to the pathogenesis of diabetic neuropathy involving large fiber and C-fiber dysfunction and which are factors well known in the art as contributing to the loss of peripheral neurological function resulting in loss of myelinated axons in diabetic patients.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claims 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennani-Kabachi et al. (V) and Bhadada et al. (U) in view of Crea et al. (US 6,416,808 B1), in light of Benavente-Garcia et al. (W).

Applicant's claimed invention was set forth above.

The combined teachings of Bennani-Kabachi and Bhadada are set forth above. As shown above in the Benavente-Garcia, an aqueous extract of olive leaves would intrinsically comprises both hydroxytyrosol and oleuropein having antioxidant activity and possessing several biological properties which are at least partially related to their antioxidant and free radical scavenging activity. The combined references teach the instantly claimed invention except for the specific recitation of the claimed weight ratio of hydroxytyrosol to oleuropein. However, it would have been obvious to one of ordinary skill in the art to modify the amounts of the hydroxytyrosol and oleuropein in the composition used in the method of treating patients with large fiber and C-fiber taught by the combined references because at the time the invention was made the administration of dietary supplements comprising hydroxytyrosol and oleuropein were well known in the art, as evidenced by the teachings of Crea. For instance, Crea teaches a dietary supplement comprising an aqueous extract of olives and having a weight ratio of hydroxytyrosol and oleuropein of between about 5:1 and about 200:1 or between about 10:1 and about 100:1. In Column 7, lines 30-40, Crea teaches that the hydroxytyrosol-rich dietary supplement can be used as a therapeutic and/or an antioxidant for health purposes. Moreover, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the

art would routinely optimize. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Crea teaches that the ratio of hydroxytyrosol to oleuropein in an olive-derived supplement can be varied. Thus, the reference recognizes that the amount of the claim-designated ingredients can be modified. Therefore, it would have been customary for an artisan of ordinary skill to determine the optimal amount of the ingredient to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

One of ordinary skill in the art would have been motivated to modify the amounts of the hydroxytyrosol and oleuropein in the composition used in the method of treating patients with large fiber and C-fiber taught by the combined references because at the time the invention was made Crea taught that olive derived extracts comprising the claim-designated ratios of hydroxytyrosol and oleuropein were useful in treating mammalian disease conditions requiring the beneficial functional antioxidant effects of hydroxytyrosol and oleuropein; and, thus the artisan of ordinary skill would have had a reasonable expectation that the modification would be a success to arrive at the claimed method of treatment because given the references as a whole the artisan would reasonably expect that the action of these compounds would exert their known therapeutic effects to attenuate the factors involved in diabetic neuropathy.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennani-Kabachi et al. (V) and Bhadada et al. (U) in view of Crea et al. (US 6,416,808 B1), in light of Benavente-Garcia et al. (W).

Applicant's claimed invention was set forth above.

The combined teachings of Bennani-Kabachi and Bhadada are set forth above. As shown above in the Benavente-Garcia, an aqueous extract of olive leaves would intrinsically comprise both hydroxytyrosol and oleuropein having antioxidant activity and possessing several biological properties which are at least partially related to their antioxidant and free radical scavenging activity. The combined references teach the instantly claimed invention except for administering an aqueous extract of olives and except for the specific recitation of the claimed weight ratio of hydroxytyrosol to oleuropein. However, the instantly claimed method of treatment would have been *prima facie* obvious to one of ordinary skill in the art because at the time the invention was made the administration of dietary supplements comprising hydroxytyrosol and oleuropein obtained from an aqueous extract of olives were well known in the art, as evidenced by the teachings of Crea. For instance, Crea teaches a dietary supplement comprising an aqueous extract of olives and having a weight ratio of hydroxytyrosol and oleuropein of between about 5:1 and about 200:1 or between about 10:1 and about

100:1. In Column 7, lines 30-40, Crea teaches that the hydroxytyrosol-rich dietary supplement can be used as a therapeutic and/or an antioxidant for health purposes. Moreover, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Crea teaches that the ratio of hydroxytyrosol to oleuropein in an olive-derived supplement can be varied. Thus, the reference recognizes that the amount of the claim-designated ingredients can be modified. Therefore, it would have been customary for an artisan of ordinary skill to determine the optimal amount of the ingredient to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

One of ordinary skill in the art would have been motivated to modify the amounts of the hydroxytyrosol and oleuropein intrinsic to the composition used in the method of treating patients with large fiber and C-fiber taught by the combined references because at the time the invention was made Crea taught that aqueous extracts of olives comprising the claim-designated ratios of hydroxytyrosol and oleuropein were useful in treating mammalian disease conditions requiring the beneficial functional antioxidant effects of hydroxytyrosol and oleuropein; and, thereby the artisan of ordinary skill would have been motivated to replace the composition used in the method taught by the

combined teachings of Bennani-Kabachi with the composition taught by Crea because the instantly claimed method of treatment would have been no more than a matter of routine optimization to provide a result effect variable for the replacement of one functional equivalent for the other wherein it would be highly reasonable to assume that compositions comprising the same or essentially the same ingredients would provide the same beneficial functional effect for treating patients with large fiber and C-fiber neuropathy, given that compositions comprising hydroxytyrosol and oleuropein were known for their free radical scavenging effects, hypoglycemic and lipid perioxidation inhibitory activities.

As each of the references indicates that the various proportions and amounts of the ingredients used in the claimed method composition are result variables, they would have been routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by each of the references.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

be referred to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele Flood
Primary Examiner
Art Unit 1655

MCF
March 28, 2009

/Michele Flood/
Primary Examiner, Art Unit 1655